

Appl. No. 09/529,575  
Amdt. Dated Sept. 8, 2003  
Reply to Office Action of May 6, 2003

### REMARKS

In the specification, the paragraph beginning at page 3, line 8 has been amended to remove "benzamidine and its salts and derivatives."

Claims 31-33, 36, 41-46, and 48-53 are pending and stand rejected in this application. Claims 31 and 36 have been amended to substitute "0.0001%" for "0.001%." Additionally, the term "article" replaces "protease inhibitor" and the term "protease inhibitor" replaces "article" within the first conjunctive phrase. Basis for the amendments may be found in the specification at page 29, lines 6-11.

Claim 42 has been amended to change "protease inhibitor" to "skin care composition" and "skin care composition" to "protease inhibitor." Support for the amendment may be found in the specification at page 32, lines 7-9. No new matter, however, has been added.

### INVENTION SYNOPSIS

The present invention is directed to an absorbent article at least a portion of which comprises a protease inhibitor, wherein the article comprises from about 0.0001% to about 30% by weight of the protease inhibitor; the protease inhibitor has an  $IC_{50}$  of about 500  $\mu M$  or less, as measured by a General Fecal Protease Method; and the protease inhibitor is selected from the group consisting of 4-(2-aminoethyl)-benzenesulfonylfluoride hydrochloride, hexamidine and its salts, pentamidine and its salts, and mixtures thereof.

Applicants have found that the protease inhibitor-treated absorbent articles inhibit fecal proteases and, therefore, reduce the skin irritation due to contact with feces and as a direct result of the inhibitor-enzyme interaction, rather than by any indirect means (e.g., change in pH, the inactivation of a cofactor required for enzyme activity, or the presence of other skin health-enhancing compounds). By the judicious selection of inhibitors, which inactivate the major types of proteases present in feces, a method for the treatment and/or prevention of diaper dermatitis is established that requires a very low amount of the protease inhibitor in the article.

### REJECTIONS UNDER 35 USC § 112, FIRST PARAGRAPH

Claims 31 and 36 stand rejected under 35 USC § 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably

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convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention. The Office states that the specification does not disclose that the article comprises from about 0.001% to about 30% by weight of protease inhibitor. The specification range is from about 0.0001% to about 30%. Applicants respectfully traverse the rejection.

In order to expedite prosecution, Applicants have amended Claims 31 and 36 to more accurately reflect the language of the specification. Claims 31 and 36 have been amended to substitute "0.0001%" for "0.001%." Applicants submit that Claims 31 and 36, as amended, reasonably convey possession of the claimed inventions, and, therefore, respectfully request withdrawal of the rejection under 35 U.S.C. § 112, first paragraph and reconsideration of the claims.

REJECTIONS UNDER 35 U.S.C. § 112, SECOND PARAGRAPH

Claims 31-33, 36, 41-46, and 48-53 stand rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claims 31 and 36 are rejected because the phrase "the protease inhibitor comprises from about 0.001% to about 30% by weight of the article" is indefinite. With respect to Claim 42, Claim 41 claims the use of a delivery system that contains the protease inhibitor. Claim 42 claims that the delivery system of Claim 41 is a skin care composition and that "the protease inhibitor comprises from about 0.01% to about 50% by weight of the skin care composition." Claim 42 is rejected because it is unclear how the protease inhibitor can comprise the delivery system. Applicants respectfully traverse the rejection.

In order to expedite prosecution, Applicants have amended Claims 31 and 36 to more accurately reflect the language of the specification. Claim 31 and 36 have been amended to switch the use of "article" and "protease inhibitor" in the relevant limitation. Claim 42 has been amended to switch the use of "skin care composition" and "protease inhibitor." As a result of amended Claims 31, 36, and 42, Applicants submit that Claims 31-33, 36, 41-46, and 47-53 particularly point out and distinctly claim the subject matter, and, therefore, respectfully request withdrawal of the rejection under 35 U.S.C. § 112, second paragraph and reconsideration of the claims.

REJECTIONS UNDER 35 USC § 103(a)

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Claims 31-33, 36, 41-46, and 48-53 stand rejected under 35 U.S.C. § 103(a) as being unpatentable over Roe (U.S. Patent No. 5,607,760) (hereafter "Roe") in view of Kasahara et al. (JP 04-182,423) (hereafter "Kasahara"). With respect to Claims 31-33, 36, 41-44, 48, 49, 51, and 52, the Office states that Roe teaches a diaper containing a topsheet coated with a semisolid lotion and immobilizing agent but fails to provide for a protease inhibitor. The Office offers that Kasahara teaches protease inhibitors in the form of a lotion or emulsion where the inhibitors include benzamidine and derivatives thereof. The Office asserts that benzamidine is an equivalent structure to pentamidine due to the fact that the active or functional group of pentamidine is the benzamidine structure. The Office surmises that it would have been obvious to one skilled in the art at the time the invention was made to use the protease inhibitor composition of Kasahara on the topsheet of Roe to reduce skin irritation and prevent diaper rash. Applicants traverse this rejection.

Applicants submit that the claims are not rendered obvious over Roe in light of Kasahara. Roe teaches a diaper containing a liquid pervious topsheet coated with a lotion composition. Kasahara discloses a composition for cleaning and wiping and containing "benzamidine, p-aminobenzamidine, m-aminobenzamidine, phenylguanidine, (2R, 4R)-4-methyl-1-[N<sup>2</sup>-(3-methyl-1,2,3,4-tetrahydro-8-quinolinesulfonyl)-L-alginy]-2-piperidine carboxylic acid monohydrate, dansylarginine N-(3-ethyl-1,5-pentanyl)amide, etc."

Applicants have previously provided a declaration under 37 C.F.R. § 1.132 distinguishing pentamidine from benzamidine based on structural dissimilarities and existence of unexpected results. See, Declaration of Scott Edward Osborne dated October 30, 2002 (hereafter "Declaration"). Applicants wish to reemphasize that a prima facie case of obviousness based on structural similarity is rebuttable by proof that the claimed compounds possess unexpectedly advantageous or superior properties. In re Papesch, 315 F.2d 927 (CCPA 1967). Applicants have provided experimental data showing the unexpectedly advantageous and superior properties of pentamidine and hexamidine over benzamidine. See, Declaration, Table 1. Pentamidine and hexamidine inhibit the rate of protease cleavage by 50% at concentrations significantly lower than that required of benzamidine. Pentamidine requires a concentration of 37  $\mu$ M and hexamidine requires a concentration of 31  $\mu$ M to inhibit protease cleavage by 50%. In contrast, benzamidine requires a concentration of 966  $\mu$ M to achieve the same result. Pentamidine

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provides the same protease inhibitory effect as benzamidine but at a concentration of about 4% of that of benzamidine. In other words, benzamidine must exist at a concentration 26-times as great as pentamidine to achieve the same result. While the burden is on the applicant to establish results that are unexpected and significant, a seven-fold increase in activity of a claimed compound over the prior art compound has been held to rebut prima facie obviousness based on close structural similarity. In re Wiechert, 370 F.2d 927 (CCPA 1967). Clearly, the Declaration shows sufficient unexpectedly advantageous and superior properties distinguishing pentamidine and hexamidine over benzamidine.

The Office discounts the Declaration because of discrepancies with the original specification and claims. The Office states that the original specification lists benzamidine as a preferred inhibitor meeting the claimed requirements for the IC<sub>50</sub> values. Additionally, the Office states that the originally presented claims have the IC<sub>50</sub> value as no more than 500  $\mu$ M as measured by the General Fecal Protease Method and that Claim 8 teaches benzamidine as one of the compounds meeting this limitation.

Applicants offer that "obviousness is determined by the totality of the record including, in some instances most significantly, the evidence and arguments proffered during the give-and-take of ex parte patent prosecution." In re Chu, 66 F.3d 292, 299 (Fed. Cir. 1995). Applicants can find no basis for the Office's implication that Applicants are somehow precluded from distinguishing subject matter forfeited during the course of prosecution. In keeping with In re Chu, Applicants offer that the totality of the record stands for the nonobviousness of pentamidine and hexamidine over benzamidine. Applicants have narrowed the scope of the claims to exclude benzamidine and have provided ample evidence of nonobviousness through the Declaration.

Furthermore, Applicants acknowledge the error in identifying benzamidine, in the original Claim 8, as a protease inhibitor with an IC<sub>50</sub> of about 500  $\mu$ M or less, as measured by a General Fecal Protease Method. The error in Claim 8, however, has been corrected through amendment, and the amendment has ample basis in the specification. Applicants' specification states, "Each of the protease inhibitors included in the absorbent articles of the invention is a chemical substance which meets at least one of the seven criteria for IC<sub>50</sub> . . ." See, page 9, line 24-29. The specification discloses that the protease inhibitors identified meet at least one of the seven criteria (i.e., Purified Protease Method for Trypsin, Chymotrypsin, and Leucine

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Aminopeptidase; Specific Decal Protease for Trypsin, Chymotrypsin, and Leucine Aminopeptidase; and General Fecal Protease). Applicants do not disclose that a protease inhibitor will meet all of the IC<sub>50</sub> criteria. In light of the Declaration, benzamidine clearly does not meet the General Fecal Protease criteria of an IC<sub>50</sub> of about 500 μM or less.

Based on the foregoing arguments, Applicants respectfully request that the Office's rejection of Claims 31-33, 36, 41-44, 48, 49, 51, and 52 for obviousness based on equivalent chemical structure be withdrawn.

With respect to Claims 45, 46, and 50, the Office states that Roe discloses the skin care composition being on the top sheet, and, therefore, it will be transferred onto the skin of the wearer by either heat or pressure. Claims 45, 46, and 50 are dependent upon and contain all the limitations of Claim 31. Applicants respectfully submit, that based upon the discussion presented above, that pentamidine and hexamidine are not equivalent to benzamidine, and that Claim 31 is nonobvious compared to the prior art. Since independent Claim 31 is nonobvious in light of the reasoning presented above, Claims 45, 46, and 50 depending there from are also nonobvious. In re Fine, 837 U.S.P.Q.2d 1596 (Fed. Cir. 1988). Therefore, Applicants respectfully request reconsideration and withdrawal of this rejection.

Claims 53 stand rejected under 35 USC § 103(a) as being unpatentable over Roe (U.S. Patent No. 5,607,760) and Kasahara et al (JP 04-182,423) in further view of VanRijswijck et al. (U.S. Patent No. 6,120,488). The Office states that Roe and Kasahara disclose the use of the skin care composition being disposed on the topsheet, but fail to disclose the use of a skin care composition being disposed in stripes on the topsheet. VanRijswijck discloses the use of a skin care composition disposed on the topsheet in a plurality of stripes. The Office concludes that it would have been obvious to one having ordinary skill in the art at the time the invention was made to have the skin care composition of Roe, be disposed in stripes, as disclosed by VanRijswijck, in order to provide unique skin care benefits to different areas of the wearer. Claim 53 is dependent upon and contains all the limitations of Claim 31. Applicants respectfully submit, that based upon the discussion presented above, that pentamidine and hexamidine are not equivalent to benzamidine, and that Claim 31 is nonobvious compared to the prior art. Since independent Claim 31 is nonobvious in light of the reasoning above, Claim 53 depending there

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from is also nonobvious. In re Fine, 837 U.S.P.Q.2d 1596 (Fed. Cir. 1988). Therefore, Applicants respectfully request reconsideration and withdrawal of this rejection

It is well settled that the Office cannot pick and choose among individual elements of assorted prior art references to recreate the claimed inventions based on the hindsight of Applicants' invention. Rather, the Office has the burden to show some teaching or suggestion in the references to support their use in the particular claimed combination. See SmithKline Diagnostics, Inc. v. Helena Lab. Corp., 8 U.S.P.Q.2d 1468, 1475 (Fed. Cir. 1985). Here, there is no such teaching or suggesting. Additionally, the mere fact that it is possible to find isolated disclosures which might be combined in such a way as to produce a new composition does not necessarily render such production obvious unless the art contains something to suggest the desirability of the proposed combination. In re Grabiak, 222 U.S.P.Q.2d 870, 872 Fed. Cir. 1985). Furthermore, "obvious to try" is not a valid test of patentability. In re Dow Chemical Co., 5 U.S.P.Q.2d 1529 (Fed. Cir. 1988); In re Antoine, 195 U.S.P.Q. 6 (CCPA 1977). There must be a suggestion or teaching that the claimed novel form could or should be prepared. In re Cofer, 148 U.S.P.Q. 268 (CCPA 1966). Thus, it is clearly the case that the present invention could not have been rendered obvious by Roc, Kasahara, or VanRijswijck or any in combination since none provide the limitations as set forth by Applicants.

#### CONCLUSION

Based on the foregoing reasons, Applicants respectfully submit that the Office has not made a prima facie case of obviousness and the rejections are therefore improper. Reconsideration and withdrawal of the rejections are respectfully requested. Allowance of each of the pending claims in the next Office Action if respectfully requested.

Respectfully Submitted,

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